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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/240,455	01/29/1999	DAVID D. MUNDSCHENK	15050.5	7348

22859 7590 11/01/2005

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EXAMINER	
BERKO, RETFORD O	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/240,455	MUNDSCHENK, DAVID D.	
	Examiner	Art Unit	
	Retford Berko	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-12,15-26,30-42,45,46,50-52,55 and 56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-12,15-26,30-42,45,46,50-52,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement: The Amendment filed 7/25/05 is acknowledged.

Status of Claims

(1) Claims 1, 3-12, 15-26, 30-42, 45, 46, 50-52 and 55-66 are currently pending.

(2) Claims 2, 13, 14, 27, 28, 29,43, 44, 47-50, 53, 54 and 67-69 were cancelled by applicant; without prejudice.

The application was re-assigned to Examiner Retford Berko for continued prosecution.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 3 remain rejected under 35 USC 102(e) as anticipated by Gizurarson et al (US 6, 514, 503; filed July 9, 1998)

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the

inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Claims 1 and 3are drawn toward a medicament delivery method, i.e. providing a delivery system that comprises a formulation of inactivated bioactive peptide and mucosal absorption enhancer (a quaternary ammonium salt, e.g. benzalkonium chloride; for enhancing mucosal absorption to buccal cavity).

Gizurarson et al (Patent '503) teaches an antigen delivery system suitable for bucally administering attenuated antigens, immunogens and toxoids including F peptide and tetanus toxoid in a formulation to subjects, said formulation comprising penetration or absorption enhancer benzalkonium chloride (abstract, col 2, lin 55-65; col 3, lin 60-65, col 6, lin 51-50; col 7, lin 5-15, col 10, lin 7-50 and col 11, lin 64-65 continuing to col 12, lin 1-35).

Claims 1 and 3 are anticipated by Patent '503.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-12, 15-26, 30-42, 45, 46, 50-52 and 55-66 remain rejected under 35 USC Sec 103(a) as unpatentable over Hale et al (US 5, 607, 691) in view of Gizurarson et al (US 6, 514, 503) further in view of Blumberg et al (US 6, 030, 613; filed July 24, 1997)

Hale et al (Patent '691) disclose enhanced delivery, by buccal administration, peptides (e.g. insulin, calcitonin, and oxytocin --col 15, lin 10-65 and col 16, lin 5-15; col 17) and toxins (col 18, lin 55-60; col 39, lin 55-67) in a formulation comprising absorption enhancers (col 46, lin 45-50; col 47, lin 45-65). According to Hale et al, the formulation can be delivered to buccal, sublingual and oral and may be formulated as aerosols (col 52, lin 40-65 and col 53, lin10-25).

Patent '691 does not teach the use of specific toxins such as notexin, crotoxin, for the formulation and does not teach the use of effective amount or the concentration of penetration enhancer.

Gizurarson et al (Patent '503) was discussed. Patent '503 discloses a delivery system suitable for administering attenuated peptides and other immunogens (e.g. F peptide and tetanus toxoid in a formulation comprising penetration or absorption enhancer benzalkonium chloride (col 2, lin 55-65; col 3, lin 60-65, col 6, lin 51-50; col 7, lin 5-15, col 10, lin 7-50 and col 11, lin 64-65 continuing to col 12, lin 1-35).

Blumberg et al (Patent '613) discloses effective final concentration of benzalkonium chloride as 0.05% (col 14, lin 30-35). Patent '613 further discloses the use of toxins (e.g. enterotoxins, cholera toxin, peptides, and drugs in formulations for oral, sublingual and buccal

delivery (col 9, lin 37-45; col 13, lin 40-55, col 16, lin 50-60; col 17, lin 40-55; col 18, lin 35-45); col 23, lin 60-67 continuing to col 24, lin 1-10).

One of ordinary skill would be motivated to prepare a medicamentdelivery system comprising attenuated peptide or toxin wherein the formulation comprising penetration enhancer or absorption promoter (e.g. benzalkonium chloride). One of ordinary skill would expect to obtain a formulation having enhanced immunogenicity, reduced toxicity and having less irritation effect on the skin as previously achieved by the prior art cited (Patent '503, col 9, lin 50-55 and col 12, lin 30-45). Therefore invention as a whole would have been prima facie obvious to one of ordinary skill at the time the invention was made.

The following prior art reference is considered pertinent to applicant's claims and is cited for the record and is not relied upon in the rejection of the claims: Watts, P. et al (WO 96/05810). Watts et al disclose a delivery composition comprising bioactive compounds that are peptides (e.g. calcitonin and insulin) (page 25, line 15-30. The delivery system, applicable to the buccal cavity also includes a penetration enhancer or absorption enhancing material—chitosan (page 26, lin 5-20). The reference is not currently used because it does not disclose the use of benzalkonium chloride as absorption enhancing agent.

Response To Arguments:

Applicant's remark and arguments have been considered but are found to be unpersuasive:

Applicant argues that the rejection under Sec 102(e) is confusing because it seems to be premised on existence of a common inventor with the instant application, and that in fact, applicant contends, there is no actual, or even apparent relationship between the two cases or their inventors.

In response, the Sec 102(e) rejection is not based upon common inventorship. Rather, Gizurarson et al (Patent '503) teaches an antigen delivery system suitable for bucally administering attenuated antigens, immunogens and toxoids including F peptide and tetanus toxoid in a formulation to subjects, said formulation comprising penetration or absorption enhancer or preservative--benzalkonium chloride (col 2, lin 55-65; col 3, lin 60-65, col 6, lin 51-50; col 7, lin 5-15, col 10, lin 7-50 and col 11, lin 64-65 continuing to col 12, lin 1-35). Claim 1 as currently presented, does not preclude an antigen delivery system that can be orally administered. There is no issue regarding common inventorship and examiner did not base the rejection on common inventorship. On the issue of lack of motivation or suggestion as asserted by applicant, examiner notes that Gizurarson et al (Patent '503) disclosed that when a drug composition in delivery device contains penetration enhancer or, there is less irritating effect (Patent '503, lin 50-58) and also the use of adjuvants enhance the ability of weakly antigenic substances and reduces the risk of toxic reactions (Patent '503, col 12, lin 35-45).

Applicant argues that the cited references fail entirely to teach or suggest even the elements of the invention as presently claimed, let alone to the extent that would be required to obviate this invention, contending that the rejection is based upon three references that each appear to be cited for the mere occurrence of various keywords somewhere within their texts.

In response, Hale et al disclosed buccal delivery system (Patent '691, col 5, lin 11 and col 52, lin 60), penetration, or permeation enhancer or absorption enhancer (col 6, lin 36-40, col 44, lin 40 and col 46, lin 50) and preservatives (e.g. benzalkonium chloride; col 47, lin 64) for delivery of peptides (Table 2 at col 15-16, col 17, lin 42), toxins (col 18, lin 56).

Blumberg et al (Patent '613) was relied upon to reinforce the fact that applicnat's invention comprising buccal delivery device for administration of peptides, antigens, toxins and preservatives is disclosed ---Blumberg disclosed buccal delivery devices (Patent '613, col 17, lin 49, col 18, lin 4, lin 32 effective final concentration of benzalkonium chloride as 0.05% (col 14, lin 30-35). Patent '613 further discloses the use of toxins (e.g. enterotoxins, cholera toxin, peptides, and drugs in formulations for oral, sublingual and buccal delivery (col 9, lin 37-45; col 13, lin 40-55, col 16, lin 50-60; col 17, lin 40-55; col 18, lin 35-45); col 23, lin 60-67 continuing to col 24, lin 1-10). The motivation to combine the prior art cited is based upon the need to reduce irritation effects of the active agents as suggested by Gizurarson et al (Patent '503).

Conclusion: No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Respectfully,

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Retford Berko** whose telephone number is571-272-0590. The examiner can normally be reached on M-F from 8.00 am to 5.30 pm

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Thurman K Page**, can be reached on 571-272-0602.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
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